

CLAIMS

What is claimed is:

1. A method of inhibiting a reverse transcriptase, comprising:

presenting the reverse transcriptase with a compound according to Formula (I)



wherein HET comprises a heterocycle;

L is a linker in which at least two atoms form a contiguous chain, wherein one of the two atoms is covalently bound to the heterocycle, and wherein another one of the two atoms is covalently bound to the carbonyl atom;

- 10 Y is O, S, or NR₃;

R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, and lower alkyl; and

R₂ is selected from the group consisting of an aryl, a cycloalkyl, a cycloalkenyl, and a heterocycle, and wherein R₂ is optionally substituted.

- 15 2. The method of claim 1 wherein HET is a substituted triazole or substituted imidazole.

3. The method of claim 2 wherein the substituted triazole or imidazole is substituted with a first substituent and a second substituent, and wherein at least one of the first and second substituents includes an aryl group.

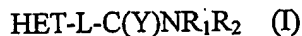
- 20 4. The method of claim 3 wherein the first substituent is methyl, CF₃, or a halogen, and wherein the second substituent is tolyl, a halogenated phenyl, or a substituted quinoline.

5. The method of claim 1 wherein L is -X₁-CR₃R₄-, wherein

X₁ is selected from the group consisting of S, O, S(O), S(O)₂, and CR₃R₄; and

R₃ and R₄ are independently hydrogen, halogen, lower alkyl, lower alkenyl, lower alkynyl, NH₂, OH, and SH.

6. The method of claim 1 wherein L is selected from the group consisting of -S-CH₂-, -S(O)-CH₂-, -S(O)₂-CH₂-, -O-CH₂-, and -CH₂-CH₂-.
- 5 7. The method of claim 1 wherein Y is O.
8. The method of claim 1 wherein R₁ is hydrogen and R₂ is a substituted aryl or substituted heteroaryl.
9. The method of claim 8 wherein R₂ comprises an ortho-substituted phenyl.
10. The method of claim 9 wherein the ortho-substituent is a halogen or a methyl.
- 10 11. The method of claim 1 wherein the reverse transcriptase is an HIV reverse transcriptase.
12. The method of claim 11 wherein the HIV reverse transcriptase is at least partially resistant to a non-nucleoside analog reverse transcriptase inhibitor.
13. The method of claim 1 wherein the step of presenting the reverse transcriptase
15 comprises *in vivo* presentation.
14. The method of claim 1 wherein the compound is converted to a prodrug before the step of presenting.
15. The method of claim 1 further comprising presenting the reverse transcriptase with a second inhibitor.
- 20 16. The method of claim 15 wherein the second inhibitor is selected from the group of a non-nucleoside reverse transcriptase inhibitor and a nucleoside reverse transcriptase inhibitor.
17. A method of treating an HIV infected patient comprising:
administering to the patient a pharmaceutical composition comprising a compound
25 according to Formula (I) at a dosage effective to reduce viral propagation;



wherein HET comprises a heterocycle;

L is a linker in which at least two atoms form a contiguous chain, wherein one of the two atoms is covalently bound to the heterocycle, and wherein another one of the two atoms is covalently bound to the carbonyl atom;

Y is O, S, or NR₃;

R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, and lower alkyl; and

R₂ is selected from the group consisting of an aryl, a cycloalkyl, a cycloalkenyl, and a heterocycle, and wherein R₂ is optionally substituted.

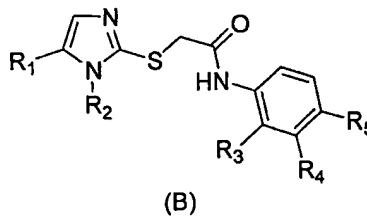
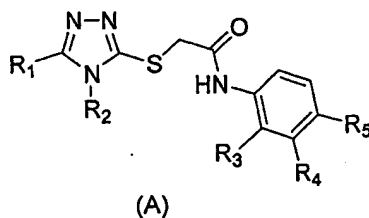
18. The method of claim 17 wherein HET is a substituted triazole or substituted imidazole.

19. The method of claim 18 wherein L is selected from the group consisting of -S-CH₂-, -S(O)-CH₂-, -S(O)₂-CH₂-, -O-CH₂-, and -CH₂-CH₂-.

20. The method of claim 18 wherein Y is O.

21. The method of claim 18 wherein R₁ is hydrogen, CF₃, or a halogen, and wherein R₂ is a substituted aryl or substituted heteroaryl.

22. The method of claim 17 wherein the compound has a structure according to Formula (A) or Formula (B)



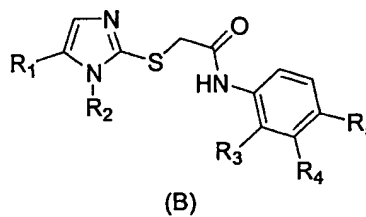
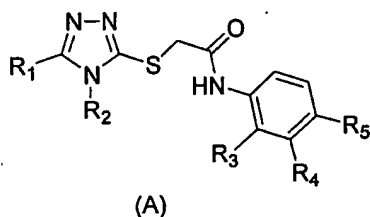
wherein R₁ is optionally substituted lower alkyl, halogen, or CF₃,

R₂ is optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted quinoline, or optionally substituted isoquinoline; and

R₃, R₄, and R₅ are independently hydrogen, halogen, optionally substituted alkyl, S-alkyl, CF₃, heterocycle, NR'R'', S(O)₂R', or C(O)R', and wherein R' and R'' are independently NH₂, NHAlkyl, NHAcyl, NAlkylAcyl, N(Alkyl)₂, O-alkyl, acyl, aryl, alkyl, heterocycle, or R' and R'' form a ring.

23. The method of claim 17 further comprising co-administering a second antiviral medicament.
24. The method of claim 23 wherein the second medicament is selected from the group of a non-nucleoside reverse transcriptase inhibitor, a protease inhibitor, a nucleoside reverse transcriptase inhibitor, an integrase inhibitor, a viral binding inhibitor, and a fusion inhibitor.
25. A pharmaceutical product, comprising:
- a compound of structure HET-L-C(Y)NR₁R₂, wherein HET comprises a heterocycle, L is a linker in which at least two atoms form a contiguous chain, wherein one of the two atoms is covalently bound to the heterocycle, and wherein another one of the two atoms is covalently bound to the carbonyl atom, Y is O, S, or NR₃, R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, and lower alkyl, R₂ is selected from the group consisting of an aryl, a cycloalkanyl, a cycloalkenyl, and a heterocycle, wherein R₂ is optionally substituted; and
- an instruction to administer the compound to a patient infected with a retrovirus under a protocol that reduces viral propagation of the retrovirus.
26. The product of claim 25 wherein HET is a substituted triazole or substituted imidazole.
27. The product of claim 26 wherein the substituted triazole or imidazole is substituted with a first substituent and a second substituent, and wherein at least one of the first and second substituents includes an aryl.

28. The product of claim 27 wherein the first substituent is methyl, halogen, or CF₃, and wherein the second substituent is tolyl, a halogenated phenyl, or a substituted quinoline.
29. The product of claim 25 wherein L is -X₁-CR₃R₄-, wherein
- 5 X₁ is selected from the group consisting of CH₂, S, O, S(O), S(O)₂, and CR₃R₄; and R₃ and R₄ are independently hydrogen, halogen, lower alkyl, lower alkenyl, lower alkynyl, NH₂, OH, and SH.
30. The product of claim 25 wherein L is selected from the group consisting of -S-CH₂-, -S(O)-CH₂-, -S(O)₂-CH₂-, -O-CH₂-, and -CH₂-CH₂-.
- 10 31. The product of claim 25 wherein R₁ is hydrogen and R₂ is a substituted aryl or substituted heteroaryl.
32. The product of claim 31 wherein R₂ comprises an ortho-substituted phenyl.
33. The product of claim 32 wherein the ortho-substituent is a halogen or a methyl.
34. The product of claim 25 wherein the compound has a structure according to Formula
- 15 (A) or Formula (B),



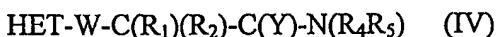
wherein R₁ is optionally substituted lower alkyl, halogen, or CF₃,

R₂ is optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted quinoline, or optionally substituted isoquinoline; and

- 20 R₃, R₄, and R₅ are independently hydrogen, halogen, optionally substituted alkyl, S-alkyl, CF₃, heterocycle, NR'R'', S(O)₂R', or C(O)R', and wherein R' and R''

are independently NH₂, NHAlkyl, NHAcyl, NAlkylAcyl, N(Alkyl)₂, O-alkyl, acyl, aryl, alkyl, heterocycle, or R' and R" form a ring..

35. A compound having a structure according to Formula (IV)



- 5 wherein HET comprises a heterocycle;

W is S(O), S(O)₂, or CH₂;

R₁ and R₂ are independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, halogen, OH, SH, NH₂, N₃, O-alkyl, or CH₂OH;

- 10 Y is O, S, or NR₃, wherein R₃ is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, or hydroxy, O-alkyl, or CH₂OH;

R₄ is hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; and

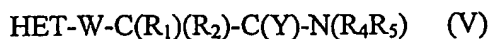
R₅ is selected from the group consisting of an aryl, a cycloalkanyl, a cycloalkenyl, and a heterocycle, and wherein R₅ is optionally substituted.

- 15 36. The compound of claim 35 wherein HET comprises a substituted triazole or a substituted imidazole.

37. The compound of claim 36 wherein R₁, R₂, and R₄ are hydrogen, and wherein R₅ is comprises an ortho-substituted phenyl.

- 20 38. The compound of claim 37 wherein Y is O, and wherein HET is substituted with at least one of an optionally substituted aryl and a substituent selected from the group consisting of a halogen, CF₃, and CH₃.

39. A compound having a structure according to Formula (V)



wherein HET comprises a heterocycle;

W is O, S, S(O), S(O)₂, or CH₂;

R_1 and R_2 are independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, halogen, OH, SH, NH_2 , N_3 , O-alkyl, or CH_2OH ;

Y is S or NR_3 , wherein R_3 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, or hydroxy, O-alkyl, or CH_2OH ;

5 R_4 is hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; and

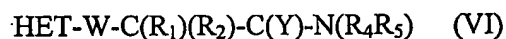
R_5 is selected from the group consisting of an aryl, a cycloalkanyl, a cycloalkenyl, and a heterocycle, and wherein R_5 is optionally substituted.

40. The compound of claim 39 wherein HET comprises a substituted triazole or a substituted imidazole.

10 41. The compound of claim 40 wherein R_1 , R_2 , and R_4 are hydrogen, and wherein R_5 is comprises an ortho-substituted phenyl.

42. The compound of claim 41 wherein Y is NR_3 .

43. A compound having a structure according to Formula (VI)



15 wherein HET comprises a disubstituted 1,2,4-triazole or a disubstituted imidazole, wherein at least one substituents of HET is a substituted aryl, and wherein the substituted aryl is covalently bound to a nitrogen of HET;

W is O, S, $S(O)$, $S(O)_2$, NH, NR_1 or CH_2 ;

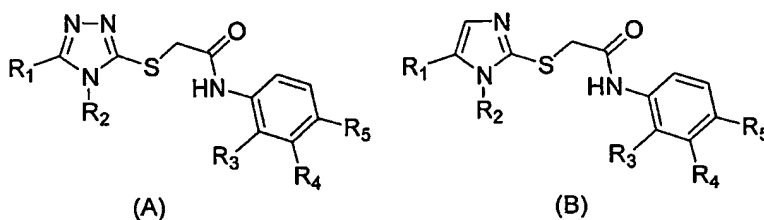
20 R_1 and R_2 are independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, halogen, OH, SH, NH_2 , N_3 , O-alkyl, or CH_2OH ;

Y is O, S, or NR_3 , wherein R_3 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, or hydroxy, O-alkyl, or CH_2OH ;

R_4 is hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; and

25 R_5 is selected from the group consisting of an aryl, a cycloalkanyl, a cycloalkenyl, and a heterocycle, and wherein R_5 is optionally substituted.

44. The compound of claim 43 wherein R_1 , R_2 , and R_4 are hydrogen, and wherein R_5 is comprises an ortho-substituted phenyl.
45. The compound of claim 44 wherein Y is O.
46. The compound of claim 43 having a structure according to Formula (A) or (B)



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wherein R_1 is optionally substituted lower alkyl, halogen, or CF_3 ,

R_2 is optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted quinoline, or optionally substituted isoquinoline; and

R_3 , R_4 , and R_5 are independently hydrogen, halogen, optionally substituted alkyl, S-alkyl, CF_3 , heterocycle, $NR'R''$, $S(O)_2R'$, or $C(O)R'$, and wherein R' and R'' are independently NH_2 , $NHAlkyl$, $NHAcyl$, $NAlkylAcyl$, $N(Alkyl)_2$, O-alkyl, acyl, aryl, alkyl, heterocycle, or R' and R'' form a ring.

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47. The compound of claim 46 wherein R_2 is selected from the group consisting of a monosubstituted phenyl, a disubstituted phenyl, a trisubstituted phenyl, a monosubstituted naphthyl, a disubstituted naphthyl, a trisubstituted naphthyl, a monosubstituted quinoline, a disubstituted quinoline, a trisubstituted quinoline, a monosubstituted isoquinoline, a disubstituted isoquinoline, and a trisubstituted isoquinoline.

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48. The compound of claim 46 wherein the at least one of the substituents of the substituted aryl is an optionally substituted lower alkyl, CF_3 , a lower alkoxy, a halogen, or $NR'R''$, wherein R' and R'' is H or lower alkyl.